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Long-term results of a prospective randomised trial assessing the impact of readaptation of the dorsolateral peritoneal layer following extended pelvic lymph node dissection and cystectomy

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Running head: Long-term outcomes of reperitonealisation after radical cystectomy

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Abstract

Objective: To evaluate the long term oncological and functional outcomes after readaptation of the dorsolateral peritoneal layer following pelvic lymph node dissection (PLND) and cystectomy .

Patients and Methods: A randomised, single-center, single-blinded, two-arm trial was conducted on 200 consecutive cystectomy patients who underwent PLND and cystectomy for bladder cancer (<cT4, cN0, cM0) between April 2006 and September 2009. Patients were randomised into two groups: group A with readaptation of the dorsolateral peritoneal layer (n=100; 73 male, 27 female; median age 68 yrs, range 35-86 yrs) and group B without readaptation (n=100; 66 male, 34 female; median age 65 yrs, range 30-86 yrs). Regular postoperative follow-up was performed at our outpatient clinic. Median follow-up was 59 months (range 3-100 months), five patients were lost to follow-up in group A, seven in group B. Bowel function was evaluated using the validated Gastrointestinal Quality of Life Index questionnaire and an institutional questionnaire regarding post-cystectomy outcome. Local recurrences and distal metastases were evaluated using computed tomography and bone scan at the regular follow-up visits.

Results: There was no significant difference between the two groups in terms of the rate of local (pelvic) recurrence (5/95 [5.3%] in group A; 7/93 [7.5%] in group B; $p = 0.53$), the rate of distant metastases (21/95 [22.1%] in group A; 23/93 [24.7%] in group B; $p = 0.67$), cancer-specific survival ($p = 0.37$), and overall survival ($p = 0.59$). Group A had significantly better bowel function at 3 ($p < 0.001$), 6 ($p < 0.006$), 12 ($p < 0.006$) and 24 months ($p = 0.04$), and significantly less postoperative abdominal pain and bloating at 3 ($p = 0.002$) and 6 months ($p = 0.01$).

Conclusion: Readaptation of the dorsolateral peritoneal layer following PLND and cystectomy has a beneficial long-term impact on bowel function and postoperative pain without compromising oncological radicality.

Keywords: bowel function; cystectomy; long-term outcomes; pelvic lymph node dissection; prospective randomised trial

Introduction

Radical cystectomy with extended pelvic lymph node dissection (PLND) and urinary diversion - the gold standard treatment for muscle invasive bladder cancer (MIBC) (1) - is a major and complex surgical procedure (2, 3). Despite improvements in anesthesia, surgical technique, and pre- and postoperative patient management it is still burdened by frequent complications. Reported early postoperative complication rates (≤ 30 days following surgery) vary from 20% to 58% in recent series (4-7). Among these complications, impairment of bowel function (16%-29%) is most common (5, 7-10). In 2011 Roth et. al. reported that readaptation of the dorsolateral peritoneum parietale at the end of the surgery led to a decrease in postoperative pain and earlier recovery of bowel function within the first 30 postoperative days (10). This procedure comprises the sparing incision and resection of the dorsolateral peritoneum parietale dorsomedially to the external iliac vessels and close to the bladder in order to create peritoneal flaps to cover the vessels at the end of the operation. Thus, the questions arise as to whether this procedure is safe from an oncological point of view and whether the finding of earlier recovery of bowel function can translate into long-term improvement of gastrointestinal function.

Patients and methods

Patients

Between April 2006 and September 2009, 200 patients undergoing (**open**) radical cystectomy, extended PLND and ileal urinary diversion due to bladder cancer (BC) at our institution were prospectively enrolled in this study. Patients were randomised by a computer-based program without stratification into two groups: group A with readaptation of the dorsolateral peritoneal layer (n=100), and group B without readaptation (n=100). Exclusion criteria were previous PLND and cT4 MIBC. Preoperative patient characteristics did not differ between the two groups (Table 1). Median follow-up was 59 months (range: 3 – 100 months). Five patients were lost to follow-up in group A, seven in group B (Figure 1). The study was conducted according to ethical standards and based on good clinical practice, and was approved by the local ethics committee. All patients gave their informed consent.

Surgical technique

The surgical technique and patient management was described in detail previously (10). Briefly, in group A the lateral peritoneum parietale was incised dorsomedially and mobilised off the external iliac vessels on both sides to maintain large peritoneal flaps for readaptation of the dorsolateral peritoneal layer at the end of surgery (**Figure 2**). In group B, the lateral peritoneum parietale was incised above the external iliac artery without creating flaps. The template of our extended PLND encompassing the obturator fossa and internal, external, and common iliac lymph nodes up to the uretero-iliac junction, and the bowel anastomosis (end to end) were standardised and did not differ between the two groups. At least one of three senior

staff members was involved in the surgeries in 97% and 99% in group A and B, respectively.

Patient management

Preoperatively, patients were given two high enemas. Oral diet was initiated on postoperative day 1 starting with fluids. It was then gradually advanced as tolerated. A combined anesthesia (general and epidural) was given intraoperatively, and epidural analgesia (1 mg/ml bupivacaine hydrochloride, 2 mcg/ml fentanyl citrate, 2mcg/ml adrenaline in NaCl 0.9%) was given postoperatively. Fluid administration intraoperatively was restricted. To prevent thrombosis low-molecular-weight heparin was injected subcutaneously into the arm starting on the evening before surgery.

Outcome measures

The trial was originally designed to evaluate early postoperative complications and postoperative pain as well as gastrointestinal function in the short and long term. Early postoperative outcomes (≤ 30 days after surgery) were already published in 2011 (10) showing an improved recovery of bowel function and fewer complications within 30 days following surgery. We are reporting in the present study the long-term follow up of this trial in terms of gastrointestinal function as primary outcome measures and survival data as secondary outcome measures.

Follow-up

Patients were followed according to our institutional follow-up protocol as described in detail earlier (11). Briefly patients had regular follow-up examinations at our outpatient clinic 3, 6, 12 and 24 months following surgery, and annually thereafter.

The clinical follow-up included computed tomography and bone scan at 6, 12 and 24 months and if clinically indicated. Local recurrences were defined as soft tissue mass ≥ 2 cm occurring within the field of PLND and cystectomy below the aortic bifurcation (which is inside the bony pelvis). Distant recurrences/metastases were defined as those occurring outside the pelvis (12, 13). At the time points 0, 3, 12 and 24 months during follow-up patients were asked to respond to the modified validated Gastrointestinal Quality of Life Index (GIQLI) questionnaire (14) documenting how often they were bothered by different bowel complaints (frequent bowel movements, urgent bowel movements, diarrhoea, constipation, and uncontrolled stool loss) as described by Fung et. al (15) (Table 2). Additionally at 3, 6, 12 and 24 months postoperatively patients were requested to complete our institutional post-cystectomy gastrointestinal outcome questionnaire regarding stool frequency, need for stool regulating medication, constipation, nausea/vomiting, and abdominal pain/bloating (Table 3).

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, version 17, Chicago, IL, USA). Data were labelled as nominal or quantitative variables. Nominal variables were characterized by means of frequencies. Quantitative variables were tested for normality of distribution applying the Kolmogorov-Smirnov test and were described by mean \pm standard deviation or median and quartiles whenever appropriate for the GIQLI and institutional questionnaires. Differences in the median between groups were analyzed using Kruskal–Wallis test. The frequencies of nominal variables were compared with the chi-square test. Intention to treat analysis provided information about survival from

the time of randomisation. Survival analysis was performed using the Kaplan Meyer method; the log-rank test was used for univariate comparisons. The level of statistical significance was set at $p < 0.05$. Sample size ($n = 100$ for each group) was initially calculated on the basis of a two-sided significance level of 5% and a power of 80% ($\alpha = 0.05$; $\beta = 0.2$) assuming that the complication rates in group A and B are 10% and 23%, respectively.

Results

Survival outcome

There were no statistically significant differences in overall survival (OS; $p = 0.59$) and cancer specific survival (CSS; $p = 0.37$) between the two groups; 5-year OS rates were 59.9% and 66.7% in groups A and B respectively, CSS rates were 78.9% and 76.5% (Figure 3 a and b). The two groups also did not differ significantly in terms of the rate of local (pelvic) recurrence (5/95 patients [5.3%] in group A; 7/93 patients [7.5%] in group B; $p = 0.53$); and the rate of distant metastases (21/95 [22.1%] in group A; 23/93 [24.7%] in group B; $p = 0.67$). Recurrence-free survival (RFS; $p = 0.64$; Figure 3c) and local recurrence-free survival (LRFS; $p = 0.61$; Figure 3d) did not differ between the two groups; RFS rates for groups A and B at one year and five years were 85.3% and 87.1 %, and 73.7%, and 71% respectively (Figure 3c)

Functional outcome

Analysis of the GIQLI questionnaire data showed a statistically significant difference between the groups in terms of constipation (at 24 months) and diarrhoea (at 3 months) in favour of group A patients (Table 2). The institutional questionnaire

showed a significantly better outcome after readaptation of the dorsolateral peritoneum (group A) in terms of gastrointestinal function (questions Q1-Q4; Table 3). Moreover, patients in group A experienced significantly less postoperative abdominal pain (question Q5) at 3 ($p = 0.002$) and 6 months ($p = 0.01$; Table 3).

Post-hoc subgroup analysis of our institutional questionnaire showed that the improvement in postoperative gastrointestinal function after readaptation of the dorsolateral peritoneal layer (group A) was more pronounced on a percentage basis in non-orthotopic neobladder patients (ileal conduit, catheterizable pouch) than in orthotopic neobladder patients, mainly during the first 6 months after surgery (Tables 4a and 4b). Subgroup analysis of the GIQLI questionnaire, again, showed better results on a percentage basis after readaptation of the dorsolateral peritoneal layer in non-orthotopic neobladder patients – although not statistically significant due to the low number of patients in this cohort (Tables 5a and 5b).

Discussion

Closure of the dorsolateral peritoneal layer has a beneficial impact on early (≤ 30 days) postoperative recovery and early complications following PLND and cystectomy (10). We could show that these encouraging short-term results translate into long-term improvement of postoperative bowel function and a reduction in postoperative pain and bloating without compromising oncological radicality.

Data on long-term gastrointestinal function after PLND and radical cystectomy is scarce and comparison of different urinary diversion techniques is always difficult due to the differences in the types and lengths of bowel segment used. Earlier studies reported bowel complications after urinary diversion in up to 24% of patients over the long-term although no validated questionnaires were used (16, 17). This is

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in line with our findings showing 29% of all cystectomy patients were bothered at least at some time by either constipation, urgent bowel movements and/or stool frequency even 24 months after surgery according to the validated Gastrointestinal Quality of Life Index Questionnaire (GIQLI) (Table 2). This number is high compared to regular “non-cystectomy” populations in which constipation is seen in 2% to 28% and irritable bowel disease in 12% (18, 19). Moreover, almost 50% of our cystectomy patients complained about postoperative abdominal pain or bloating and needed medication for stool regulation after 3 months (Table 3). This is important information that must be borne in mind when informing patients about the consequences of PLND, cystectomy and urinary diversion. However, as shown in this study, gastrointestinal function can be improved by small measures such as readaptation of the dorsolateral peritoneum parietale to cover the iliac vessels. Just why gastrointestinal function improves after reperitonealisation, however, is not fully understood, neither for the early postoperative period nor in the long-term. The underlying mechanisms are probably multifactorial. A major factor, however, might be a reduction in the number of intra-abdominal adhesions to the pelvic wall and iliac vessels resulting from the resection of the covering layer (peritoneum parietale) leading at worst to palsy, kinking of bowel segments, constipation, and/or mechanical ileus. Other possible factors underlying the impaired postoperative gastrointestinal function – at least in the earlier postoperative period - might be an inhibitory sympathetic input due to elevated stress reaction, metabolic acidosis with a reactive palsy, and/or a release of neurotransmitters, hormones and/or inflammatory mediators that might lead to disorganized electrical activity and a lack of coordinated propulsion and which therefore might inhibit the motility of the gastrointestinal tract (20-24). Because preoperative and postoperative patient management was the same

in both groups, we do not think that these factors may have influenced the gastrointestinal outcomes.

Interestingly, subgroup analysis revealed that patients with a non-orthotopic diversion (ileal conduit and catheterizable pouch) in particular benefited most from readaptation of the dorsolateral peritoneal layer; whereas fewer than 8% of patients after reperitonealisation complained of constipation 3 months postoperatively irrespective of the urinary diversion, one third of patients complained after non-orthotopic diversion in the group without reperitonealisation versus only 20% after orthotopic neobladder in this group (Table 4). As a consequence, after reperitonealisation 20% of patients needed stool-regulating medication 3 months postoperative irrespective of the urinary diversion, whereas 80% of patients with non-orthotopic diversion needed this medication compared to only 40% of patients with orthotopic neobladder without reperitonealisation (Table 4). This difference is probably due to the fact that in orthotopic neobladder patients the empty space left by resection of the bladder (and to some extent the pelvic lymph nodes) is partly covered by the bladder substitute itself, thus leaving much less open wound surface in the pelvis, whereas in patients with non-orthotopic diversions small bowel loops may adhere more easily to the wound surface without reperitonealisation possibly leading to obstruction and delayed gastrointestinal passage.

Since surgical factors such as the number of lymph nodes removed and positive surgical margins influence BC outcomes and especially the rate of local recurrences (25), our major concern regarding the present procedure was that sparing of peritoneum parietale dorsomedially to the external iliac vessels might leave tumour (cells) – detectable only microscopically – in situ which would have fatal consequences for the patient in terms of RFS and CSS. Our long-term follow-up,

however, found comparable or even favorable rates of local and distal recurrences, and no differences in RFS, CSS, and OS compared to other cohorts (26). It can be concluded that reperitonealisation is a safe procedure that does not compromise oncological safety and radicality. It is of utmost importance, however, that the peritoneum is not incised too medially on the tumour-bearing side and thus too close to the bladder tumour. The local recurrences rates observed were 5.3% and 7.5% in the groups with and without reperitonealisation, respectively. These rates are lower than the 7% to 15% rates usually reported (13, 25, 27, 28). Interestingly, most local recurrences occurred within 18 months of surgery, although some did occur later than 2 years postoperatively (Figure 3d). This finding underscores the importance of close follow-up not only during the first 12 to 24 months following surgery, but also thereafter (11).

While a clear benefit in short and long term could be shown after readaptation of the dorsolateral peritoneal layer in open radical cystectomy, PLND and urinary diversion, the question arises whether it impacts functional recovery following minimally-invasive surgery. Although purely speculative, we do not see any reason why the benefit of improved postoperative results should not translate into the outcomes of minimally-invasive techniques, in particular since the template of PLND should be the same irrespective of the surgical technique. In addition, a more dorsal incision of the lateral peritoneum parietale to create peritoneal flaps can be performed easily in minimally-invasive surgery.

A major limitation of this study is that a considerable number of patients did not return the questionnaires. However, return rates of 60% (GIQLI) and 80% (institutional post-cystectomy questionnaire) are reasonable numbers and in line with returned questionnaire rates in other studies (29, 30). Although return rates of a

single questionnaire may have been better, patients were additionally asked to fill out our institutional questionnaire because it also assesses pain and serious gastrointestinal morbidity (e.g. hospitalisation or surgery for bowel obstruction).

Another potential limitation is the low number of patients with ileal conduit and catheterizable pouch (only 37 % in group A and 35 % in group B), meaning post-hoc subgroup analysis of different urinary diversions could be underpowered. However, the differences between orthotopic and non-orthotopic diversions within the questionnaires were large and clinically plausible. Furthermore, confounding factors such as co-medication which might influence bowel function to some extent were not routinely assessed in the long term. However, randomisation should create comparable groups and thus minimize confounding. Indeed, all baseline characteristics did not differ between group A and group B patients.

In conclusion, readaptation of the dorsolateral peritoneal layer following PLND, cystectomy and urinary diversion is a safe procedure that does not compromise oncological radicality. The procedure has a beneficial long-term impact on bowel function, and leads to a decrease in postoperative pain and bloating 3 and 6 months postoperatively.

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Conflicts of interest and financial disclosures

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Table 1

Patient characteristics

	Group A (n = 100)	Group B (n = 100)	P value
Gender, n (%)			
Male	73 (73)	66 (66)	0.28
Female	27 (27)	34 (34)	
Median age, yrs (range)	68 (35 - 86)	65 (30 - 86)	0.17
Median BMI (range)	26.2 (19-41)	25.3 (18-40)	0.75
Diabetes, n (%)	9 (9)	9 (9)	1
Chronic constipation, n (%)	12 (12)	9 (9)	0.53
Prior abdominal surgery, n (%)	34 (34)	22 (22)	0.06
Neoadjuvant chemotherapy, n (%)	16 (16)	19 (19)	0.58
Adjuvant chemotherapy, n (%)	10 (10)	9 (9)	0.81
Median operative time, min (range)	390 (195-490)	390 (225-480)	0.76
Urinary diversion, n (%)			
Ileal conduit	35 (35)	29 (29)	0.27
Orthotopic bladder substitute	63 (63)	65 (65)	
Catheterizable pouch	2 (2)	6 (6)	
Tumor stage, n (%)			
pTis/pTa	7 (7)	7 (7)	0.56
pT1	13 (13)	21 (21)	
pT2	29 (29)	30 (30)	
pT3	41 (41)	32 (32)	
pT4	10 (10)	10 (10)	
Lymph node involvement, n (%)			
pN0	75 (75)	70 (70)	0.43
pN+	25 (25)	30 (30)	

Table 2

Gastrointestinal function according to the Gastrointestinal Quality of Life Index Questionnaire (GIQLI)

	0 months		3 months		12 months		24 months	
How often during the past 2 weeks have you been troubled by:	Group A n=56	Group B n=60	Group A n=49	Group B n=58	Group A n=41	Group B n=46	Group A n=27	Group B n=31
Q1: Stool frequency								
all the time (0)	1.8 %	0 %	0 %	1.7 %	0 %	2.2 %	0 %	0 %
most of the time (1)	1.8 %	1.7 %	0 %	3.4 %	4.9 %	6.5 %	3.7 %	3.2 %
sometimes (2)	8.9 %	5.0 %	12.2 %	6.9 %	9.8 %	19.6 %	14.8 %	22.6 %
rarely (3)	23.2 %	35.0 %	22.4 %	25.9 %	24.4 %	15.2 %	25.9 %	3.2 %
never (4)	64.3 %	58.3 %	65.3 %	62.1 %	61.0 %	56.5 %	55.6 %	71.0 %
P value	0.63		0.53		0.51		0.07	
Q2: Urgent bowel movements								
all the time (0)	0 %	1.7 %	0 %	0 %	0 %	0 %	0 %	3.2 %
most of the time (1)	1.8 %	3.3 %	2.0 %	5.2 %	0 %	4.3 %	11.1 %	0 %
sometimes (2)	16.1 %	23.3 %	12.2 %	22.4 %	19.5 %	23.9 %	11.1 %	25.8 %
rarely (3)	16.1 %	26.7 %	34.7 %	24.1 %	31.7 %	26.1 %	33.3 %	29.0 %
never (4)	66.1 %	45.0 %	51.0 %	48.3 %	48.8 %	45.7 %	44.4 %	41.9 %
P value	0.19		0.37		0.61		0.16	
Q3: Diarrhea								
all the time (0)	1.8 %	0 %	0 %	0 %	0 %	0 %	3.7 %	0 %
most of the time (1)	1.8 %	0 %	0 %	3.4 %	0 %	6.5 %	0 %	3.2 %
sometimes (2)	8.9 %	6.7 %	26.5 %	10.3 %	17.1 %	17.4 %	18.5 %	12.9 %
rarely (3)	21.4 %	21.7 %	16.3 %	37.9 %	26.8 %	26.1 %	25.9 %	22.6 %
never (4)	66.1 %	71.7 %	57.1 %	48.3 %	56.1 %	50.0 %	51.9 %	61.3 %
P value	0.80		0.008		0.46		0.79	
Q4: Constipation								
all the time (0)	0 %	1.7 %	2.0 %	3.4 %	0 %	6.5 %	0 %	3.2 %
most of the time (1)	7.1 %	8.3 %	2.0 %	5.2 %	7.3 %	0 %	7.4 %	3.2 %
sometimes (2)	10.7 %	23.3 %	10.2 %	19.0 %	2.4 %	6.5 %	3.7 %	22.6 %
rarely (3)	16.1 %	11.7 %	28.6 %	25.9 %	19.5 %	26.1 %	22.2 %	35.5 %
never (4)	66.1 %	55.0 %	57.2 %	46.6 %	70.7 %	60.9 %	66.7 %	35.5 %
P value	0.32		0.59		0.09		0.04	
Q5: Uncontrolled stool loss								
all the time (0)	0 %	0 %	0 %	0 %	0 %	0 %	0 %	3.2 %
most of the time (1)	0 %	0 %	0 %	0 %	0 %	4.3 %	7.4 %	0 %
sometimes (2)	3.6 %	1.7 %	2.0 %	3.4 %	2.4 %	0 %	3.7 %	6.5 %
rarely (3)	3.6 %	8.3 %	6.1 %	10.3 %	4.9 %	6.5 %	7.4 %	12.9 %
never (4)	92.9 %	90.0 %	91.8 %	86.2 %	92.7 %	89.1 %	81.5 %	77.4 %
P value	0.50		0.70		0.53		0.53	

Table 3

Postoperative gastrointestinal function according to our institutional post-cystectomy questionnaire

	3 months		6 months		12 months		24 months	
	Group A n=78	Group B n=85	Group A n=72	Group B n=78	Group A n=56	Group B n=61	Group A n=46	Group B n=49
Q1:How often do you have stool/day?								
none	9.0 %	37.6 %	6.9 %	25.6 %	1.8 %	21.3 %	6.5 %	24.5 %
once	60.3 %	38.8 %	63.9 %	46.2 %	62.5 %	52.5 %	52.2 %	49.0 %
more than once	30.7 %	23.6 %	29.2 %	28.2 %	35.7 %	26.2 %	41.3 %	26.5 %
P value	0.0001		0.005		0.005		0.04	
Q2:Did you need medication for stool regulation?								
no	79.5 %	50.6 %	91.7 %	60.3 %	89.3 %	63.9 %	89.1 %	69.4 %
yes	20.5 %	49.4 %	8.3 %	39.7 %	10.7 %	36.1 %	10.9 %	30.6 %
P value	0.0002		0.0001		0.006		0.04	
Q3:As a consequence of constipation you needed?								
0 (no constipation)	93.6 %	75.3 %	97.2 %	78.2 %	96.4 %	85.2 %	95.7 %	83.7 %
1 (to see doctor)	6.4 %	18.8 %	2.8 %	16.7 %	1.8 %	11.5 %	4.3 %	16.3 %
2 (go to hospital)	0 %	5.9 %	0 %	3.8 %	1.8 %	3.3 %	0 %	0 %
3 (have surgery)	0 %	0 %	0 %	1.3 %	0 %	0 %	0 %	0 %
P value	0.0004		0.006		0.0001		0.057	
Q4:Do you often feel nausea or need to vomit?								
never	96.2 %	80.0 %	93.1 %	82.1 %	94.6 %	90.2 %	93.5 %	91.8 %
rarely	0 %	2.4 %	0 %	2.6 %	3.6 %	3.3 %	4.3 %	2.1 %
often	3.8 %	17.6 %	6.9 %	15.3 %	1.8 %	6.5 %	2.2 %	6.1 %
P value	0.007		0.05		0.44		0.52	
Q5:Do you often feel abdominal pain or bloating?								
never	79.5 %	54.1 %	83.3 %	65.4 %	82.1 %	75.4 %	89.1 %	81.7 %
rarely	5.1 %	15.3 %	1.4 %	10.3 %	0 %	3.3 %	0 %	6.1 %
often	15.4 %	30.6 %	15.3 %	24.4 %	17.9 %	21.3 %	10.9 %	12.2 %
P value	0.002		0.01		0.44		0.31	

Table 4

a) Postoperative gastrointestinal function according to our institutional post-cystectomy questionnaire for *non-orthotopic neobladder* patients (ileal conduit and catheterizable pouch)

	3 months		6 months		12 months		24 months	
Questionnaire	Group A n=25	Group B n=27	Group A n=23	Group B n=21	Group A n=14	Group B n=13	Group A n=13	Group B n=10
Q1:How often do you have stool/day?								
none	16.0 %	55.6 %	17.4 %	33.3 %	7.1 %	23.1 %	15.4 %	40.0 %
once	64.0 %	29.6 %	60.9 %	47.6 %	64.3 %	61.5 %	38.5 %	40.0 %
more than once	20.0 %	14.8 %	21.7 %	19.0 %	28.6 %	15.4 %	46.2 %	20.0 %
P value	0.01		0.47		0.43		0.29	
Q2:Did you need medication for stool regulation?								
no	80.0 %	29.6 %	91.3 %	38.1 %	78.6 %	46.2 %	76.9 %	50.0 %
yes	20.0 %	70.4 %	8.7 %	61.9 %	21.4 %	53.8 %	23.1 %	50.0 %
P value	0.0001		0.0001		0.08		0.17	
Q3:As a consequence of constipation you needed?								
0 (no constipation)	92.0 %	66.7 %	100 %	71.4 %	100 %	76.9 %	100 %	80.0 %
1 (to see doctor)	8.0 %	25.9 %	0 %	23.8 %	0 %	15.4 %	0 %	20.0 %
2 (go to hospital)	0 %	7.4 %	0 %	4.8 %	0 %	7.7 %	0 %	0 %
3 (have surgery)	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
P value	0.06		0.02		0.16		0.09	
Q4:Do you often feel nausea or need to vomit?								
never	96 %	66.7 %	91.3 %	81.0 %	92.9 %	92.3 %	84.6 %	80.0 %
rarely	0 %	3.7 %	0 %	4.8 %	0 %	0 %	7.7 %	10.0 %
often	4.0 %	29.6 %	8.7 %	14.3 %	7.1 %	7.7 %	7.7 %	10.0 %
P value	0.01		0.46		0.95		0.95	
Q5:Do you often feel abdominal pain or bloating?								
never	72.0 %	37.0 %	78.3 %	57.1 %	78.6 %	76.9 %	92.3 %	90.0 %
rarely	12.0 %	18.6 %	0 %	9.5 %	0 %	7.7 %	0 %	10.0 %
often	16.0 %	44.4 %	21.7 %	33.3 %	21.4 %	15.4 %	7.7 %	0 %
P value	0.03		0.17		0.54		0.35	

b) Postoperative gastrointestinal function according to our institutional post-cystectomy questionnaire for orthotopic neobladder patients

	3 months		6 months		12 months		24 months	
Questionnaire	Group A n=53	Group B n=58	Group A n=49	Group B n=57	Group A n=42	Group B n=48	Group A n=33	Group B n=39
Q1:How often do you have stool/day?								
none	5.7 %	29.3 %	2.0 %	22.8 %	0 %	20.8 %	3.0 %	20.5 %
once	58.5 %	43.1 %	65.3 %	45.6 %	61.9 %	50.0 %	57.6 %	51.3 %
more than once	35.8 %	27.6 %	32.7 %	31.6 %	38.1 %	29.2 %	39.4 %	28.2 %
P value	0.004		0.005		0.007		0.07	
Q2:Did you need medication for stool regulation?								
no	79.2 %	60.3 %	91.8 %	68.4 %	92.9 %	68.8 %	93.9 %	74.4 %
yes	20.8 %	39.7 %	8.2 %	31.6 %	7.1 %	31.2 %	6.1 %	25.6 %
P value	0.0001		0.005		0.004		0.02	
Q3:As a consequence of constipation you needed?								
0 (no constipation)	94.3 %	79.3 %	95.9 %	80.7 %	95.2 %	87.5 %	93.9 %	84.6 %
1 (to see doctor)	6.7 %	15.5 %	4.1 %	14.0 %	2.4 %	10.4 %	6.1 %	15.4 %
2 (go to hospital)	0 %	5.2 %	0 %	3.5 %	2.4 %	2.1 %	0 %	0 %
3 (have surgery)	0 %	0 %	0 %	1.8 %	0 %	0 %	0 %	0 %
P value	0.03		0.11		0.31		0.21	
Q4:Do you often feel nausea or need to vomit?								
never	96.2 %	86.2 %	93.9 %	82.4 %	95.2 %	89.6 %	97.0 %	94.9 %
rarely	0 %	1.7 %	0 %	1.8 %	2.4 %	2.1 %	3.0 %	0 %
often	3.8 %	12.1	6.1 %	15.8 %	2.4 %	8.3 %	0 %	5.1 %
P value	0.17		0.18		0.47		0.23	
Q5:Do you often feel abdominal pain or bloating?								
never	83.0 %	62.1 %	85.7 %	68.4 %	83.3 %	75.0 %	87.9 %	79.5 %
rarely	1.9 %	13.8 %	2.0 %	10.5 %	0 %	2.1 %	0 %	5.1 %
often	15.1 %	24.1 %	12.2 %	21.1 %	16.7 %	22.9 %	12.1 %	15.4 %
P value	0.01		0.07		0.47		0.37	

Table 5

Gastrointestinal function according to Gastrointestinal Quality of Life Index Questionnaire

(GIQLI) in

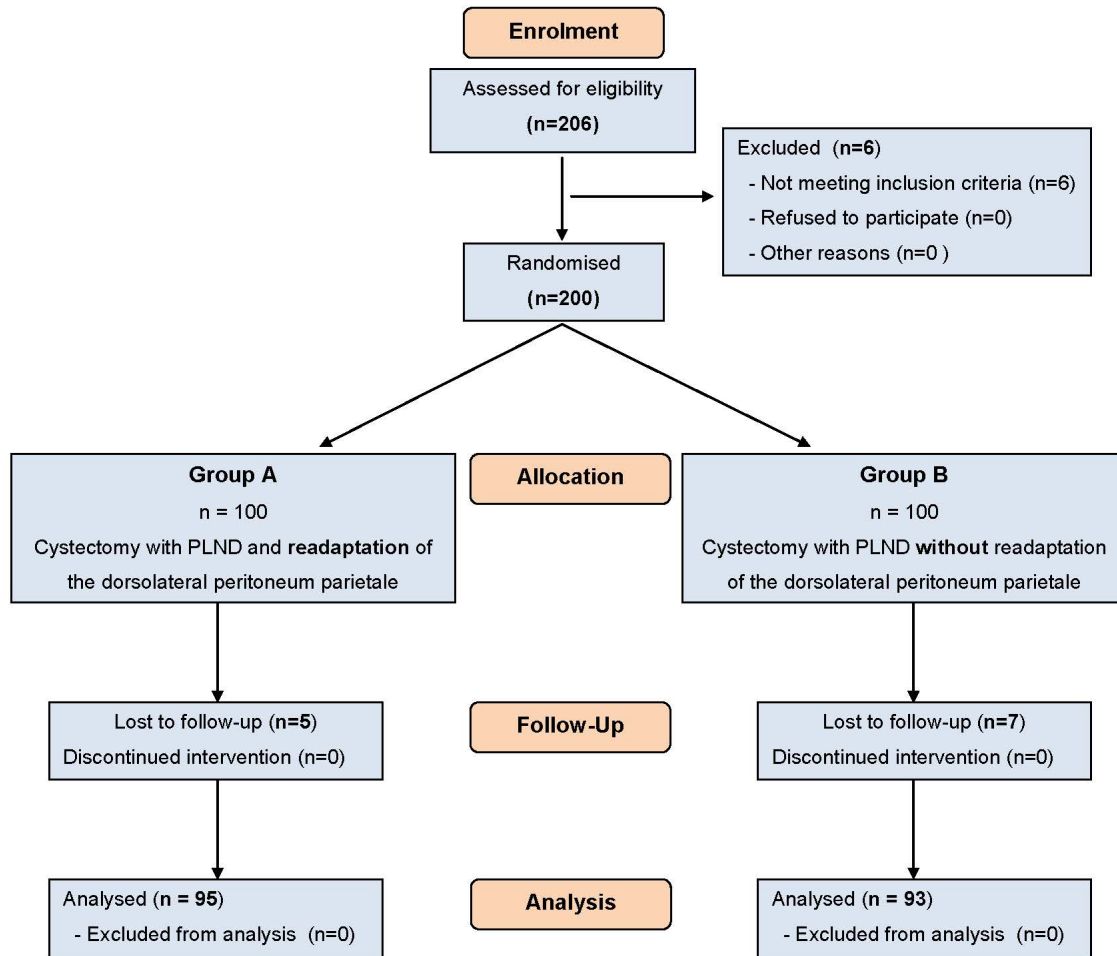
a) Non-orthotopic neobladder patients (ileal conduit, catheterizable pouch)

GIQLI Questionnaire	0 months		3 months		12 months		24 months	
How often during the past 2 weeks have you been troubled by:	Group A n=18	Group B n=18	Group A n=13	Group B n=16	Group A n=10	Group B n=14	Group A n=5	Group B n=8
Q1: Stool frequency								
all the time (0)	5.6 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
most of the time (1)	0 %	0 %	0 %	6.2 %	0 %	14.3 %	0 %	0 %
sometimes (2)	5.6 %	0 %	7.7 %	12.5 %	0 %	7.1 %	0 %	37.5 %
rarely (3)	16.7 %	38.9 %	23.1 %	25 %	60 %	24.4 %	40 %	0 %
never (4)	72.2 %	61.1 %	69.2 %	56.2 %	40 %	57.1 %	60 %	62.5 %
P value	0.26		0.75		0.18		0.14	
Q2: Urgent bowel movements								
all the time (0)	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
most of the time (1)	0 %	0 %	7.7 %	0 %	0 %	0 %	0 %	0 %
sometimes (2)	11.1 %	33.3 %	7.7 %	25.0 %	20.0 %	28.6 %	20.0 %	50.0 %
rarely (3)	11.1 %	16.7 %	23.1 %	25.0 %	30.0 %	35.7 %	20.0 %	25.0 %
never (4)	77.8 %	50.0 %	61.5 %	50.0 %	50.0 %	35.7 %	60.0 %	25.0 %
P value	0.24		0.49		0.77		0.76	
Q3: Diarrhea								
all the time (0)	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
most of the time (1)	0 %	0 %	0 %	6.2 %	0 %	14.3 %	0 %	12.5 %
sometimes (2)	16.7 %	0 %	15.4 %	6.2 %	10.0 %	14.3 %	20.0 %	12.5 %
rarely (3)	11.1 %	27.8 %	23.1 %	25.0 %	20.0 %	14.3 %	20.0 %	25.0 %
never (4)	72.2 %	72.2 %	61.5 %	62.5 %	70.0 %	57.1 %	60.0 %	50.0 %
P value	0.16		0.70		0.62		0.84	
Q4: Constipation								
all the time (0)	0 %	0 %	7.7 %	12.5 %	0 %	7.1 %	0 %	12.5 %
most of the time (1)	11.1 %	11.1 %	7.7 %	6.2 %	10.0 %	0 %	20.0 %	12.5 %
sometimes (2)	11.1 %	27.8 %	7.7 %	0 %	10.0 %	0 %	0 %	12.5 %
rarely (3)	22.2 %	11.1 %	30.7 %	31.3 %	20.0 %	28.6 %	20.0 %	37.5 %
never (4)	55.6 %	50.0 %	46.2 %	50 %	60.0 %	64.3 %	60.0 %	25.0 %
P value	0.56		0.84		0.58		0.91	
Q5: Uncontrolled stool loss								
all the time (0)	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
most of the time (1)	0 %	0 %	0 %	0 %	0 %	14.3 %	20.0 %	0 %
sometimes (2)	11.1 %	0 %	0 %	12.5 %	10.0 %	0 %	20.0 %	12.5 %
rarely (3)	5.6 %	5.6 %	7.7 %	6.2 %	0 %	7.1 %	0 %	25.0 %
never (4)	83.3 %	94.4 %	92.3 %	81.2 %	90.0 %	78.6 %	60.0 %	62.5 %
P value	0.34		0.41		0.30		0.53	

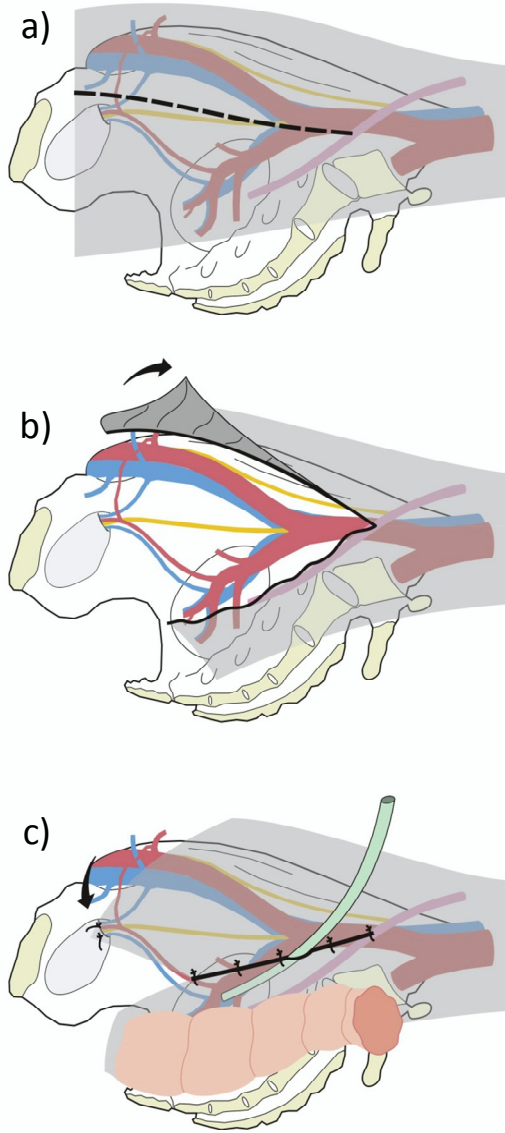
b) *Orthotopic neobladder patients*

GIQLI Questionnaire	0 months		3 months		12 months		24 months	
How often during the past 2 weeks have you been troubled by:	Group A n=38	Group B n=42	Group A n=36	Group B n=39	Group A n=30	Group B n=30	Group A n=22	Group B n=23
Q1: Stool frequency								
all the time (0)	0 %	0 %	0 %	2.6 %	0 %	0 %	0 %	0 %
most of the time (1)	2.6 %	2.4 %	0 %	2.6 %	6.7 %	0 %	4.5 %	4.3 %
sometimes (2)	10.5 %	7.1 %	13.9 %	2.6 %	13.3 %	26.7 %	18.2 %	17.4 %
rarely (3)	26.3 %	33.3 %	22.2 %	25.6 %	13.3 %	13.3 %	22.7 %	4.3 %
never (4)	60.5 %	57.1 %	63.9 %	66.7 %	66.7 %	60.0 %	54.5 %	73.9 %
P value	0.84		0.26		0.34		0.32	
Q2: Urgent bowel movements								
all the time (0)	0 %	2.4 %	0 %	0 %	0 %	0 %	0 %	4.3 %
most of the time (1)	2.6 %	4.8 %	0 %	7.7 %	0 %	6.7 %	13.6 %	0 %
sometimes (2)	18.4 %	19.0 %	13.9 %	20.5 %	20.0 %	20.0 %	9.1 %	17.4 %
rarely (3)	18.4 %	31.0 %	38.9 %	23.1 %	33.3 %	23.3 %	36.4 %	30.4 %
never (4)	60.5 %	42.9 %	47.2 %	48.7 %	46.7 %	50.0 %	40.9 %	47.8 %
P value	0.50		0.21		0.52		0.29	
Q3: Diarrhea								
all the time (0)	2.6 %	0 %	0 %	0 %	0 %	0 %	4.5 %	0 %
most of the time (1)	2.6 %	0 %	0 %	2.6 %	0 %	3.3 %	0 %	0 %
sometimes (2)	5.3 %	9.5 %	30.6 %	12.8 %	20.0 %	16.7 %	18.2 %	13.0 %
rarely (3)	26.3 %	19.0 %	13.9 %	41.0 %	26.7 %	30.0 %	27.3 %	21.7 %
never (4)	63.2 %	71.4 %	55.6 %	43.6 %	53.3 %	50.0 %	50.0 %	65.2 %
P value	0.54		0.02		0.66		0.61	
Q4: Constipation								
all the time (0)	0 %	2.4 %	0 %	0 %	0 %	3.3 %	0 %	0 %
most of the time (1)	5.3 %	7.1 %	0 %	2.6 %	6.7 %	0 %	4.5 %	0 %
sometimes (2)	10.5 %	21.4 %	11.1 %	23.1 %	0.0 %	10.0 %	4.5 %	26.1 %
rarely (3)	13.2 %	11.9 %	27.8 %	25.6 %	20.0 %	26.7 %	22.7 %	34.8 %
never (4)	71.1 %	57.1 %	61.1 %	48.7 %	73.3 %	60.0 %	68.2 %	39.1 %
P value	0.57		0.38		0.12		0.04	
Q5: Uncontrolled stool loss								
all the time (0)	0 %	0 %	0 %	0 %	0 %	0 %	0 %	4.3 %
most of the time (1)	0 %	0 %	0 %	0 %	0 %	0 %	4.5 %	0 %
sometimes (2)	0 %	2.4 %	2.8 %	0 %	0 %	0 %	0 %	4.3 %
rarely (3)	2.6 %	9.5 %	5.6 %	12.8 %	6.7 %	3.3 %	9.1 %	8.7 %
never (4)	97.4 %	88.1 %	91.7 %	87.2 %	93.3 %	96.7 %	86.4 %	82.6 %
P value	0.27		0.33		0.55		0.56	

Figure 1



Group A
with readaptation



Group B
without readaptation

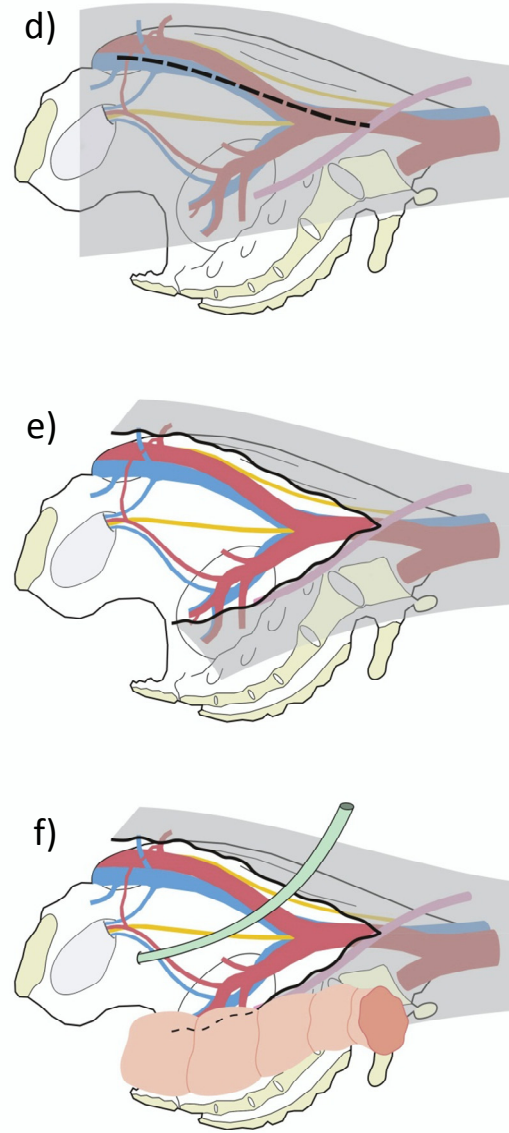


Figure 3